

### **REMARKS**

Claims 1-5, 7-9, 11, 13, and 15-22 are currently pending in the application.

Claims 10 and 14 have been cancelled without prejudice or disclaimer, solely to expedite patent prosecution in accordance with the U.S. Patent Office Business Goals (65 Fed. Reg. 54604 (September 8, 2000)). Applicant reserves the right to present the cancelled claims in a co-pending application.

Claims 1, 5, 8, 11, 13, and 15-22 have been amended for clarity, to more fully encompass Applicant's invention, and to expedite patent prosecution in accordance with the U.S. Patent Office Business Goals (65 Fed. Reg. 54604 (September 8, 2000)). Applicant reserves the right to present any cancelled subject matter in a co-pending application.

Claim 1 has been amended to recite "...an agent selected from the group consisting of: (a) compounds having an NO group and having a hypoxia relieving and smooth muscle constriction relieving effect with the said NO group being bound in said compound so it does not form NO<sub>2</sub>, NO, N<sub>2</sub>O<sub>3</sub>, N<sub>2</sub>O<sub>4</sub>, OONO<sup>-</sup> and OONO• and any products of their interaction with NO or NO<sub>2</sub>; and (b) N<sub>2</sub>O<sub>3</sub>..." (See, *inter alia*, page 8, line 20 to page 9, line 3 of the originally filed application).

Claim 5 has been amended to recite "...where the halogen is selected from the group consisting of chlorine and fluorine." (See, *inter alia*, page 9, lines 10 and 15, Example I, and Example IV of the originally filed application).

Claim 8 has been corrected by replacing "nitrosoglutathione" with "S-nitrosoglutathione." (See, *inter alia*, page 6, lines 2-6 of the originally filed application).

Claim 11 has been amended to recite "...where the disorder is selected from the group consisting of pulmonary hypertension, primary pulmonary hypertension, secondary pulmonary hypertension, and persistent pulmonary hypertension of the newborn." (See, *inter alia*, page 8, lines 2-3 and 11-13; and Examples I and V of the originally filed application).

Claim 13 has been amended to recite "...where the disorder is pneumonia or ventilation pneumonia." (See, *inter alia*, page 8, lines 2-3 and 13-15; and Examples IV and VII of the originally filed application).

Claim 15 has been amended to recite "...where the disorder is selected from the group consisting of interstitial lung diseases, including pulmonary fibrosis, and cystic fibrosis." (See, *inter alia*, page 8, lines 2-3 and 13-15; and Examples IV, IX, XI, and XII of the originally filed application).

Claim 16 has been amended to recite "...where the disorder is asthma" (See, *inter alia*, page 8, lines 2-3 and 11-13; and Examples III and X of the originally filed application).

Claim 17 has been amended to recite "...where the disorder is adult respiratory distress syndrome." (See, *inter alia*, page 8, lines 2-3 and 13-15; and Examples II, VI, and VIII of the originally filed application).

Claim 18 has been amended to recite "...where the agent comprises HNO." (See, *inter alia*, Example XI of the originally filed application).

Claim 19 has been amended to recite "...where the agent comprises NOCl or NOCN." (See, *inter alia*, page 9, line 15 and Examples I and II of the originally filed application).

Claim 20 has been amended to recite "...where the agent comprises a compound selected from the group consisting of methylnitrososulfinate, methylthionitrite, thionitroschloronitrite, and thionyl dinitrite." (See, *inter alia*, page 9, lines 12-19 and Example III, IV, V, and VI of the originally filed application).

Claim 21 has been amended to recite "...where the agent comprises trifluoronitromethane or methylnitrite" (See, *inter alia*, page 9, lines 8-11 of the originally filed application).

Claim 22 has been amended to recite "...where the agent comprises ethylnitrite" (See, *inter alia*, page 9, lines 4-7 and Examples VII, VIII, IX, and XII of the originally filed application).

These amendments are supported by the application as originally filed, and do not constitute new matter. Specific support for the amendments is shown in parentheses, above. Entry of these amendments in the application is respectfully requested.

#### **Claim objection**

In the Office Action, the Examiner has stated that if claim 19 is found allowable, claim 20 will be objected to under 37 C.F.R. § 1.75 as being substantially duplicative (Office Action, page 2). The subject matter of claim 20 to which this objection was raised has been cancelled without prejudice or disclaimer as a result of this Amendment (see above). Withdrawal of this objection is respectfully requested.

Claims 4, 5, and 17 have been objected to as being dependent on a rejected based claim, but are considered allowable by the Examiner if rewritten in independent form (Office Action, page 6). In this Amendment, the allowable subject matter of claim 17 has been incorporated into independent claim 1 to expedite patent prosecution (see above). Claims 4 and 5 are ultimately dependent on claim 1 as currently amended. Withdrawal of this objection is respectfully requested.

#### **Rejection under 35 U.S.C. §112, First Paragraph –Written Description**

Claims 21 and 22 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement (Office Action, page 2). The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed (Office Action, page 2).

Applicant respectfully traverses this rejection. The rejected subject matter of claims 21 and 22 has been cancelled without prejudice or disclaimer as a result of this Amendment (see above). Withdrawal of this ground of rejection is respectfully requested.

**Rejection under 35 U.S.C. §112, First Paragraph – Disclosed Gases**

Claims 1-3, 7-9, and 14-15 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement (Office Action, page 2). The Examiner has stated that the specification for the instant application does not provide reasonable enablement for gasses that have not been specifically disclosed, and therefore does not enable a person skilled in the art to practice the invention commensurate in scope with the claims (Office Action, pages 2-3).

Applicant respectfully traverses this rejection. To expedite patent prosecution, claim 14 has been cancelled without prejudice or disclaimer and claim 1 has been amended to incorporate the allowable subject matter of claim 17 in accordance with the Examiner's suggestion (see above). As currently amended, claim 1 reads:

1. A method for treating a pulmonary disorder associated with depletion of the S-nitrosoglutathione pool in the lung or depletion of the glutathione pool in the lung or production of reactive oxygen species in the lung of a patient having such disorder which comprises delivering into the lungs of said patient as a gas, a therapeutically effective amount of an agent selected from the group consisting of: (a) compounds having an NO group and having a hypoxia relieving and smooth muscle constriction relieving effect with the said NO group being bound in said compound so it does not form NO<sub>2</sub>, NO, N<sub>2</sub>O<sub>3</sub>, N<sub>2</sub>O<sub>4</sub>, OONO<sup>-</sup> and OONO• and any products of their interaction with NO or NO<sub>2</sub>; and (b) N<sub>2</sub>O<sub>3</sub>, which causes repletion or increase of the S-nitrosoglutathione pool in the lung or protects against toxicity where glutathione is depleted in the lung or where reactive oxygen species are increased in the lung and does so independently of reaction with oxygen.

Regarding this rejection, the Examiner has suggested that Applicant claim those specific compounds that have been identified in the specification as suitable agents for administration as gasses, including ethyl nitrite, methyl nitrite, trifluoronitrosomethane, methylnitrososulfinate, methylthionitrite, thionitrosochloronitrite, thionyldinitrite, NOCl, NOCN, and HNO (Office Action mailed August 25, 2003, page 3). As presently amended, claims 4, 5, and 18-22 read:

4. The method of Claim 1 where the agent comprises NOX where X is halogen or hydrogen.
5. The method of Claim 4 where the halogen is selected from the group consisting of chlorine and fluorine.
18. The method of Claim 1 where the agent comprises HNO.
19. The method of Claim 1 where the agent comprises NOCl or NOCN.
20. The method of Claim 1 where the agent comprises a compound selected from the group consisting of methylnitrososulfinate, methylthionitrite, thionitrosochloronitrite, and thionyldinitrite.
21. The method of Claim 1 where the agent comprises trifluoronitrosomethane or methylnitrite.
22. The method of claim 1 where the agent comprises ethylnitrite.

Amended claims 2-5, 7-9, 11, 13, and 15-22 are ultimately dependent on claim 1 as presented herein. Based on the foregoing, Applicant respectfully requests reconsideration of the rejected claims and withdrawal of this ground of rejection.

**Rejection under 35 U.S.C. §112, First Paragraph – Hydrogen Sulfide**

Claims 10-11, 13-16, and 18-20 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement (Office Action, page 4). The Examiner has stated that the specification for the instant application does not provide reasonable enablement for treatment methods involving hydrogen sulfide (Office Action, pages 2-3).

Applicant respectfully traverses this rejection. To expedite patent prosecution, claims 10 and 14 have been cancelled by this Amendment without prejudice or disclaimer (see above). Amended claims 2-5, 7-9, 11, 13, and 15-22 are ultimately dependent on claim 1 as shown herein. Withdrawal of this ground of rejection is respectfully requested.

As noted above, Applicant reserves the right to present this cancelled subject matter in a co-pending application, and respectfully submits herewith Exhibits 1-5, in support thereof, as part of the record of the instant application.

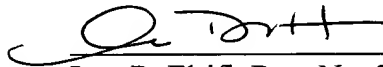
Inventor: Jonathan S. Stamler  
U.S. Application Serial No. 09/782,077

**CONCLUSION**

Applicant believes that the claims as amended are patentable and a prompt allowance is respectfully requested. If further discussion of this case is deemed helpful, the Examiner is encouraged to contact the undersigned at the telephone number provided below, and is assured of full cooperation in progressing the instant claims to allowance. Applicant believes no further fee is due at this time; however, the Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Reference Number: 28195-502 CIP (Customer Number: 35437).

Date: April 23, 2004

Respectfully submitted,



Ivor R. Elrifi, Reg. No. 39,529  
Caryn DeHoratius, Reg. No. 45,881  
Attorney/Agent for Applicant  
MINTZ, LEVIN, COHN, FERRIS  
GLOVSKY AND POPEO, P.C.  
666 Third Avenue, 24th Floor  
New York, New York 10017  
Telephone: (212) 935-3000  
Telefax: (212) 983-3115